Short communication

Aids-related primary CNS non-Hodgkin’s lymphoma in a patient with previous Epstein-Barr virus panuveitis. A clinico-pathological report

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A B S T R A C T

Clinical case: Patient with AIDS and Epstein-Barr virus (EBV) uveitis. The PCR of the aqueous and vitreous humor was positive for EBV, and DNA quantification was 56.602 × 10^6 copies/ml in the vitreous humor, 173,400 copies/ml in the peripheral blood, and negative in the cerebrospinal fluid (CSF). The patient developed a non-Hodgkin’s lymphoma (NHL), diagnosed in the autopsy.

Conclusion: The EBV is a rare cause of uveitis and it may be necessary to perform a quantitative PCR to reach the diagnosis. High amounts of EBV DNA are associated with a greater incidence of NHL.

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2173-5794/© 2014 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.
Linfoma no-Hodgkin primario del sistema nervioso central asociado a sida en un paciente con panuveítis por virus Epstein-Barr. Reporte clínico-patológico

Resumen

Caso clínico: Paciente con sida y uveítis por virus Epstein-Barr (VEB). La PCR de VEB fue positiva para humor acuoso y vítreo. Las cuantificaciones del virus fueron $56,602 \times 10^6$ copias/ml en humor vítreo, $173,400$ copias/ml en sangre periférica y negativo en líquido cefalorraquideo (LCR). El paciente desarrolló un linfoma no-Hodgkin (LNH) diagnosticado en la necropsia.

Conclusión: La uveítis por VEB es poco frecuente y para el diagnóstico es necesario realizar una PCR cuantitativa. Una elevada cantidad de DNA de VEB se ha asociado con mayor incidencia de LNH.

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Introduction

Infectious uveitis account for 11–21% of uveitis in developed countries. Characteristic ocular fundus findings are identified to diagnose infectious uveitis cases due to toxoplasma, herpes simplex virus, cytomegalovirus (CMV) and varicella-zoster virus. In patients with AIDS, the expression of these or other pathogens generally exhibit atypical signs. Early identification of causative agents is important to establish early treatment and prevent irreversible ocular damage.

The case of a patient with AIDS and posterior uveitis caused by the Epstein-Barr virus (EBV) is presented.

Clinic case

Male, 37 years, ADVP, HIV-positive since 20 years ago in discontinued antiretroviral treatment, with 206 CD4+/mm$^3$ and viral HIV load of 135,720 copies/ml. Known positive serology for toxoplasma and hepatitis B and C, splenectomy and infectious mononucleosis 7 years ago.

The patient was admitted due to pneumonia caused by Pneumocystis jirovecii treated with trimethoprim-sulfamethoxazole (240/1200 mg/6 h) and 6-methylprednisolone (20 mg/6 h), with diminished visual acuity in the left eye (LE) starting one month earlier. Funduscopy showed two areas of whitish elevated chorioretinitis with poorly defined edges in the posterior pole, with perilesional vasculitis and severe vitritis (Figs. 1 and 2). Bacteriological culture and PCR for Toxoplasma in accuracy humor were negative and Multiplex PCR for virus of the herpes group (VGH) was positive for EBV. The patient received ganciclovir (GCV) 300 mg/12 h during 15 days. Due to poor response to the treatment, posterior vitrectomy was performed and vitreous samples were taken, administering intravitreous foscarnet (2.4 mg/0.1 ml) and subsequently intravenous (100 mg/12 h). Vitreous PCR confirmed positive for EBV, with a quantification of $56,602 \times 10^6$ copies/ml. In the peripheral blood, EBV PCR was of $173,400$ copies/ml and LCR negative. Flow cytometry did not reveal malignant cells and cytology was not conclusive.

Fig. 1 – Left eye fundus, showing 2 loci of active chorioretinitis in posterior pole with perilesional vasculitis and severe vitritis.

Fig. 2 – Left eye fundus, 15 days after initiating treatment with ganciclovir. Poor response to treatment is evident, with persistence of the active chorioretinitis locus.
The patient requested voluntary release. Sixteen months later he was admitted due to right hemiparesis. Cranial CAT revealed two lesions in the corpus callosum, one in the left front lobe with mass effect and perilesional edema. LE funduscopy showed retinal necrosis with optic atrophy, without vitritis. Due to suspected cerebral toxoplasmosis, treatment was initiated with sulfadiazine (1000 mg/6 h), pyrimethamine (50 mg/24 h) and dexamethasone (4 mg/6 h), with improvement of the edema. The patient died 3 weeks later.

The necropsy evidenced B-type large cell non-Hodgkin lymphoma (NHL) in SNC. Tumor tissue detected EBER ARN due to on-site hybridization.

**Discussion**

The patient exhibited clinic compatible with uveitis is due to VGH, toxoplasma or intraocular lymphoma, requiring the inclusion of acute retinal and progressive outer retina necrosis in the differential diagnostic. Ocular involvement due to EBV Israel and occurs in the context of infectious mononucleosis.

VGH PCR in intraocular fluids is highly sensitive and specific with aqueous humor being the sample of choice at uveitis onset, with vitrectomy being carried out only in case of negative result or severity. This was the procedure adopted with the present patient.

Intraocular detection due to EBV should be interpreted prudently. In the presence of inflammatory components, viral genomic can be released when destroying infected B lymphocytes. In the present case, a high amount of EBV DNA in the vitreous was proof of ocular infection.

Qualitative Multiplex PCR is useful for screening herpetic ocular infections. Quantitative PCR enables confirmation/dismissal of EBV infection.

Treating intraocular infections due to EBV is difficult. Monotherapy with acyclovir (ACV) or GCV is efficient in intravenous followed by oral administration. However, in VIH+ cases, it could be necessary to combine ACV/GCV with foscarnet. In the present case, the combination of drugs was incomplete due to patient noncompliance.

The presence of EBV is common in AIDS-related NHL. It occurs in 100% of primary SNC lymphomas (LPSCN) and 33–65% of systemic large cell cases. Intraocular lymphoma is a subtype of LPSCN, and occurs more frequently in immunodepressed patients.

SNC NHL should be discarded in immunodepressed patients exhibiting retinitis or multifocal uveitis, with presence of VEB. In the present case, neither flow cytometry nor vitreous humor cytology facilitated the diagnostic.

Cytopathology only confirms 14–20% of the lymphomas caused by ocular infiltration of cerebral lymphoma. When intraocular lymphoma is suspected, NMR must be carried out together with LCR cytopathology prior to microbiological analysis of ocular fluids.

It is recommended to perform GH PCR in any atypical uveitis in HIV patients. Positive PCR of intraocular fluids will confirm the diagnostic, but a negative result does not exclude infection. In case of aqueous humor negativity and severe uveitis, vitrectomy should be performed. When EBV DNA is detected, viral quantification should be performed, comparing ocular fluids, peripheral blood and LCR for diagnostic confirmation.

**Conflict of interests**

The authors have declared no conflict of interests.

**REFERENCES**